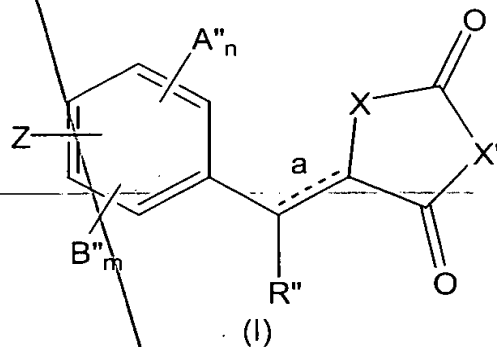
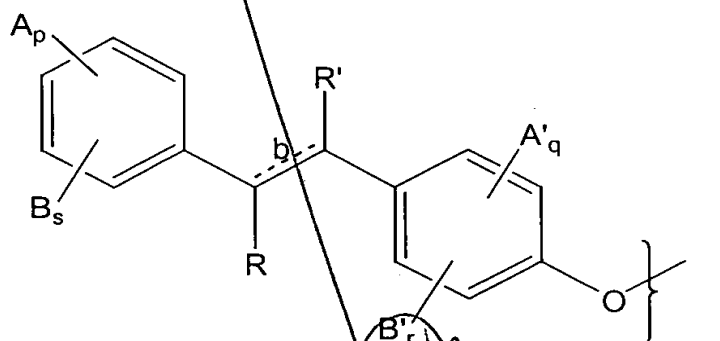


What is claimed is:

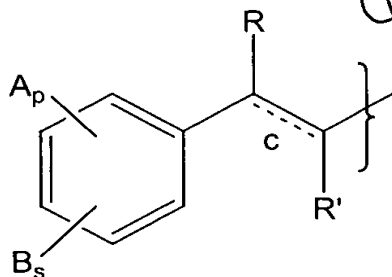
1. A compound of a formula I:



wherein Z is



H; A''; B''; or



- 5 n, m, q and r are independently integers from zero to 4 provided that $n + m \leq 4$ and $q + r \leq 4$; p and s are independently integers from zero to 5 provided that $p + s \leq 5$; a, b and c are double bonds which may be present or absent;

when present; the double bonds may be in the E or Z configuration and, when absent, the resulting stereocenters may have the R- or S- configuration;

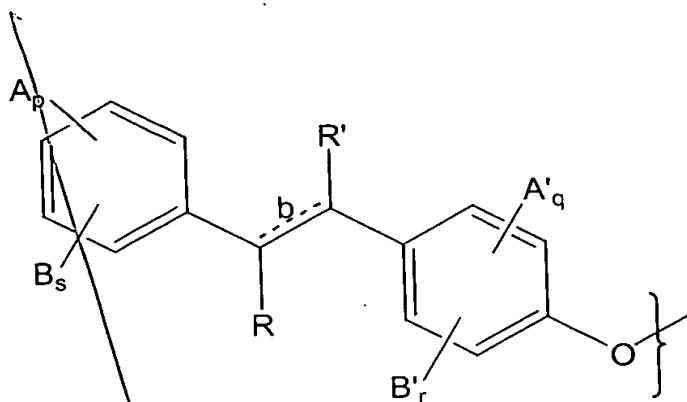
R, R' and R'' are independently H, C₁-C₂₀ linear or branched alkyl, C₂-C₂₀ linear or branched alkenyl, -CO₂Z', wherein Z' is H, sodium, potassium, or other pharmaceutically acceptable counter-ion such as calcium, magnesium, ammonium, tromethamine, and the like; -CO₂R''', -NH₂, -NHR''', -NR₂'', -OH, -OR''', halo, substituted C₁-C₂₀ linear or branched alkyl or substituted C₂-C₂₀ linear or branched alkenyl, wherein R''' is C₁-C₂₀ linear or branched alkyl or linear or branched alkenyl;

A, A' and A'' are independently H, C₁-C₂₀ acylamino; C₁-C₂₀ acyloxy; C₁-C₂₀ alkanoyl; C₁-C₂₀ alkoxy; C₁-C₂₀ alkoxy; C₁-C₂₀ alkylamino; C₁-C₂₀ alkylcarboxylamino; carboxyl; cyano; halo; hydroxy;

B, B' and B'' are independently H; C₁-C₂₀ acylamino; C₁-C₂₀ acyloxy; C₁-C₂₀ alkanoyl; C₁-C₂₀ alkenoyl; C₁-C₂₀ alkoxy; C₁-C₂₀ alkoxy; C₁-C₂₀ alkylamino; C₁-C₂₀ alkylcarboxylamino; aroyl, aralkanoyl; carboxyl; cyano; halo; hydroxy;

or A and B together, or A' and B' together, or A'' and B'' together, may be joined to form a methylenedioxy or ethylenedioxy group; and X, X' are independently -NH, -NR''', O or S.

2. A compound according to claim 1, wherein Z is

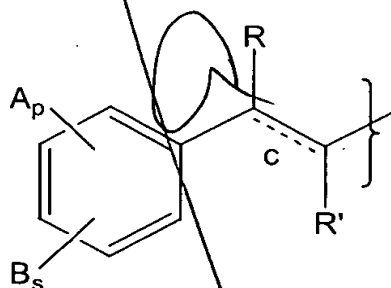


3. A compound according to claim 1, wherein Z is hydrogen.

4. A compound according to claim 1, wherein Z is A''.

5. A compound according to claim 1, wherein Z is B''.

6. A compound according to claim 1, wherein Z is

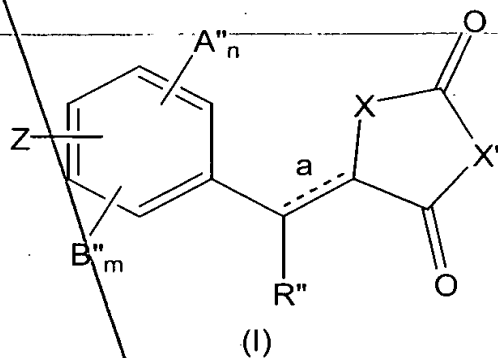


7. A compound according to claim 2, wherein X is sulfur, X' is -NH; A''_n, B'', B', A_p, A'_q, R and R'' are all hydrogen.

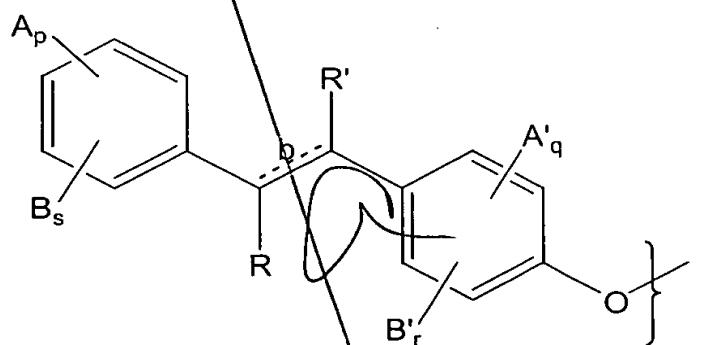
8. A compound according to claim 7, wherein B is methoxy, s is 2 and R' is carbomethoxy.

9. A compound according to claim 8, which is 5-(4-(4-(1-carbomethoxy-2-(3,5-dimethoxy phenyl) ethenyl)-phenoxy)-benzyl)-2,4-thiazolidinedione.

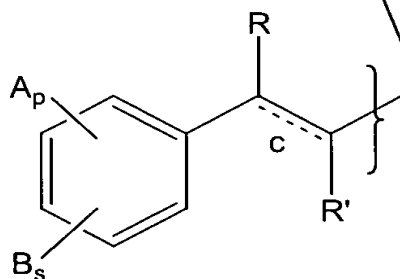
5 10. A pharmaceutical composition comprising a therapeutically effective amount of a compound of the formula I:



wherein Z is



H; A''; B''; or



n, m, q and r are independently integers from zero to 4 provided that $n + m \leq 4$ and $q + r \leq 4$; p and s are independently integers from zero to 5 provided that $p + s \leq 5$; a, b and c are double bonds which may be present or absent; when present, the double bonds may be in the E or Z configuration and, when
5 absent, the resulting stereocenters may have the R- or S- configuration;

---R, R' and R'' are independently H, C₁-C₂₀ linear or branched alkyl, C₂-C₂₀ linear or branched alkenyl, -CO₂Z', where Z' is H, sodium, potassium, or other pharmaceutically acceptable counter-ion such as calcium, magnesium,
10 ammonium, tromethamine, and the like; -CO₂R''', -NH₂, -NHR''', -NR₂'', -OH, -OR''', halo, substituted C₁-C₂₀ linear or branched alkyl or substituted C₂-C₂₀ linear or branched alkenyl, wherein R''' is C₁-C₂₀ linear or branched alkyl or linear or branched alkenyl;

15 A, A' and A'' are independently H, C₁-C₂₀ acylamino;
C₁-C₂₀ acyloxy; C₁-C₂₀ alkanoyl;
C₁-C₂₀ alkoxycarbonyl; C₁-C₂₀ alkoxy;
C₁-C₂₀ alkylamino; C₁-C₂₀ alkylcarboxylamino; carboxyl; cyano;
halo; hydroxy;

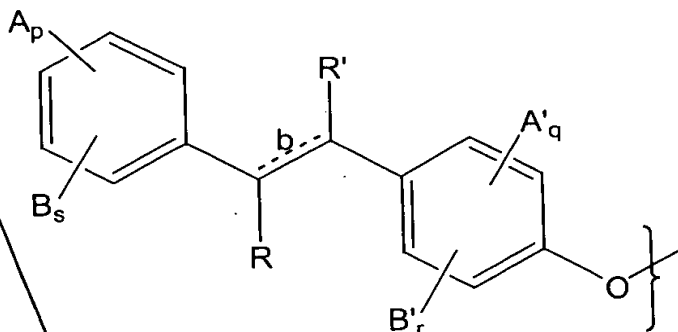
20 B, B' and B'' are independently H;
C₁-C₂₀ acylamino; C₁-C₂₀ acyloxy; C₁-C₂₀ alkanoyl;
C₁-C₂₀ alkenoyl; C₁-C₂₀ alkoxycarbonyl;
C₁-C₂₀ alkoxy; C₁-C₂₀ alkylamino;
25 C₁-C₂₀ alkylcarboxylamino; aroyl, aralkanoyl; carboxyl; cyano; halo;
hydroxy;

or A and B together, or A' and B' together, or A'' and B'' together, may be joined to form a methylenedioxy or ethylenedioxy group; and

X, X' are independently -NH, -NR''', O or S.

30 in a physiologically acceptable carrier.

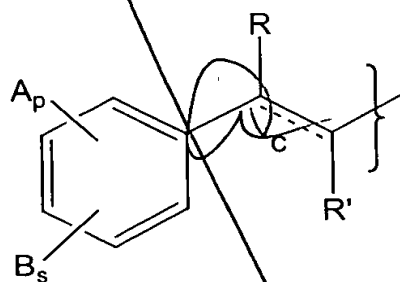
11. A composition according to claim 10, wherein Z is



12. A composition according to claim 10, wherein Z is A''.

13. A composition according to claim 10, wherein Z is B''.

14. A composition according to claim 10, wherein Z is

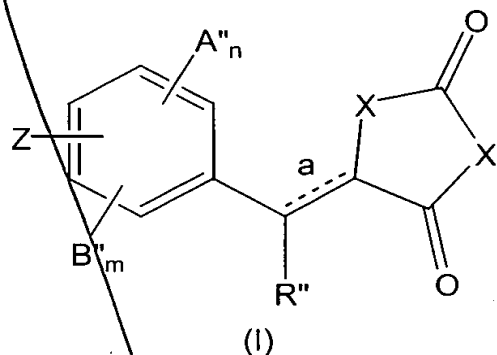


15. A composition according to claim 10, wherein X is sulfur, X' is -NH and A'', B'', A'_q, B', A_p, R and R'' are all hydrogen.

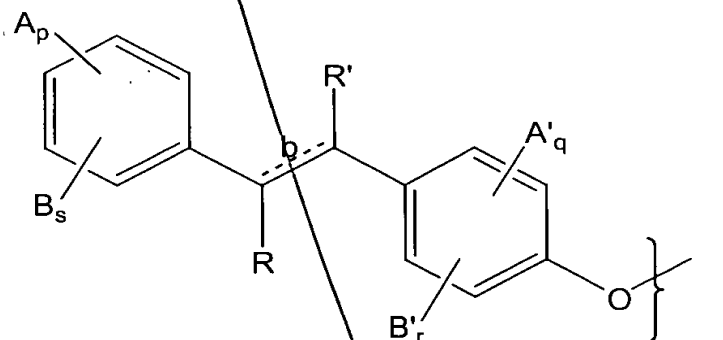
16. A composition according to claim 15, wherein R' is carbomethoxy; B is methoxy and s is 2.

17. A composition according to claim 16, wherein said compound is 5-(4-(4-(1-carbomethoxy-2-(3,5 dimethoxy phenyl) ethenyl) -phenoxy)-benzyl)-2,4-thiazolidinedione.

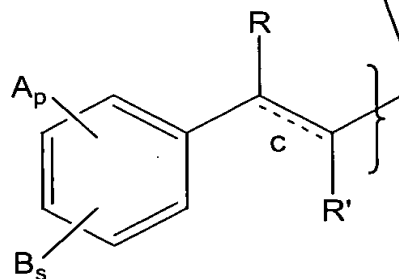
- 5 18. A method of treating diabetes comprising the steps of administering to a subject suffering from a diabetic condition, a therapeutically effective amount of a compound according to the formula I:



wherein Z is



H; A''; B''; or



n, m, q and r are independently integers from zero to 4 provided that $n + m \leq 4$ and $q + r \leq 4$; p and s are independently integers from zero to 5 provided that $p + s \leq 5$; a, b and c are double bonds which may be present or absent; when present, the double bonds may be in the E or Z configuration and, when absent, the resulting stereocenters may have the R- or S- configuration;

10 R, R' and R'' are independently H, C₁-C₂₀ linear or branched alkyl, C₂-C₂₀ linear or branched alkenyl, -CO₂Z', where Z' is H, sodium, potassium, or other pharmaceutically acceptable counter-ion such as calcium, magnesium, ammonium, tromethamine, and the like; -CO₂R''', -NH₂, -NHR''', -NR₂'', -OH, -OR''', halo, substituted C₁-C₂₀ linear or branched alkyl or substituted C₂-C₂₀ linear or branched alkenyl, wherein R''' is C₁-C₂₀ linear or branched alkyl or linear or branched alkenyl;

A, A' and A'' are independently H, C₁-C₂₀ acylamino;

C₁-C₂₀ acyloxy; C₁-C₂₀ alkanoyl;

20 C₁-C₂₀ alkoxy; C₁-C₂₀ alkoxy;

C₁-C₂₀ alkylamino; C₁-C₂₀ alkylcarboxylamino; carboxyl; cyano;

halo; hydroxy;

B, B' and B'' are independently H;

25 C₁-C₂₀ acylamino; C₁-C₂₀ acyloxy; C₁-C₂₀ alkanoyl;

C₁-C₂₀ alkenoyl; C₁-C₂₀ alkoxy;

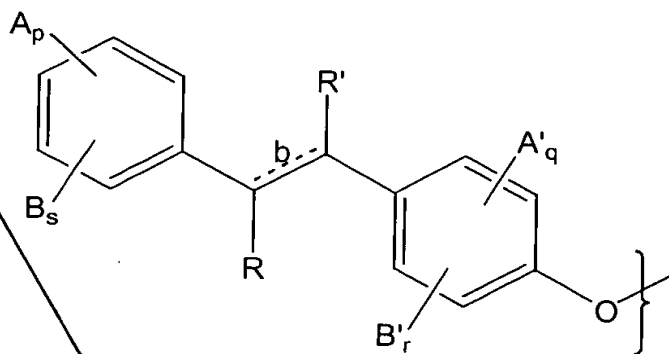
C₁-C₂₀ alkylamino; C₁-C₂₀ alkylamino;

C₁-C₂₀ alkylcarboxylamino; aroyl, aralkanoyl; carboxyl; cyano; halo;

hydroxy;

or A and B together, or A' and B' together, or A'' and B'' together, may be joined to form a methylenedioxy or ethylenedioxy group; and X, X' are independently -NH, -NR''', O or S, in a physiologically acceptable carrier.

19. A method according to claim 18, wherein Z is

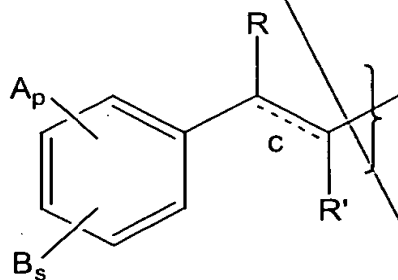


20. A method according to claim 19, wherein Z is H.

21. A method according to claim 18, wherein Z is A''.

22. A method according to claim 18, wherein Z is B''.

23. A method according to claim 18, wherein Z is



24. A method according to claim 18, wherein R'', A'', B'', A', B', A_p and R are all hydrogen, X is sulfur and X' is NH.

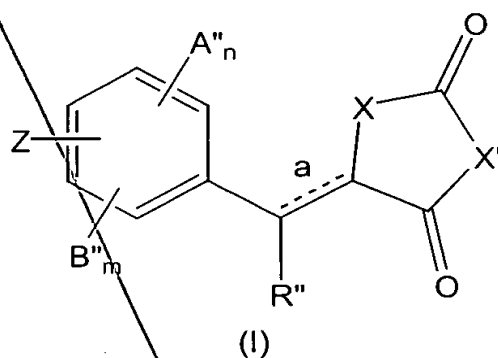
5 25. A method according to claim 18, wherein R'' is carbomethoxy and B is methoxy and s is 2.

26. A method according to claim 18, wherein said compound is 5-(4-(4-(1-carbomethoxy-2-)3,5-dimethoxy phenyl) ethenyl)-phenoxy)-benzyl)-2,4-thiazolidinedione.

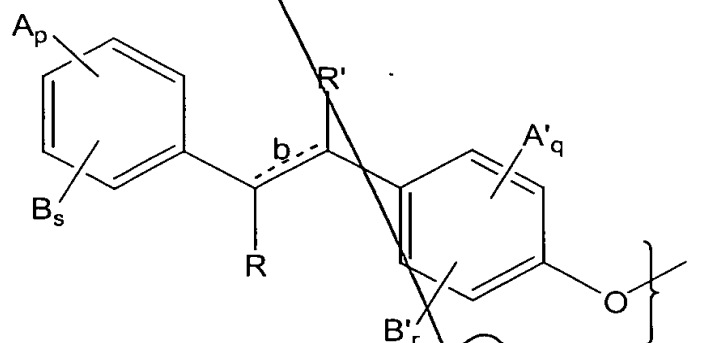
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27. A method of treating inflammation comprising the steps of administering to a subject suffering from an inflammatory condition, a therapeutically effective amount of a compound according to the formula I:

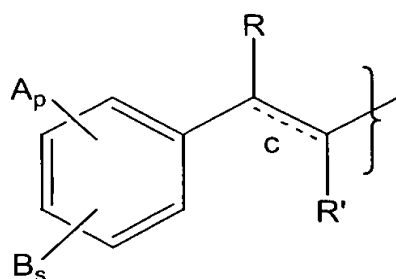
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wherein Z is



H; A''; B''; or



- 5 n, m, q and r are independently integers from zero to 4 provided that $n + m \leq 4$ and $q + r \leq 4$; p and s are independently integers from zero to 5 provided that $p + s \leq 5$; a, b and c are double bonds which may be present or absent; when present, the double bonds may be in the E or Z configuration and, when absent, the resulting stereocenters may have the R- or S- configuration;

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R, R' and R'' are independently H, C₁-C₂₀ linear or branched alkyl, C₂-C₂₀ linear or branched alkenyl, -CO₂Z', where Z' is H, sodium, potassium, or other pharmaceutically acceptable counter-ion such as calcium, magnesium, ammonium, tromethamine, and the like; -CO₂R''', -NH₂, -NHR''', -NR₂'', -OH, -OR''', halo, substituted C₁-C₂₀ linear or branched alkyl or substituted C₂-C₂₀ linear or branched alkenyl, wherein R''' is C₁-C₂₀ linear or branched alkyl or linear or branched alkenyl;

A, A' and A'' are independently H, C₁-C₂₀ acylamino;

C₁-C₂₀ acyloxy; C₁-C₂₀ alkanoyl;

C₁-C₂₀ alkoxy; C₁-C₂₀ alkoxy; C₁-C₂₀ alkoxy; C₁-C₂₀ alkoxy;

C₁-C₂₀ alkylamino; C₁-C₂₀ alkylcarboxylamino; carboxyl; cyano;

halo; hydroxy;

B, B' and B'' are independently H,

C₁-C₂₀ acylamino; C₁-C₂₀ acyloxy; C₁-C₂₀ alkanoyl;

C₁-C₂₀ alkenoyl; C₁-C₂₀ alkoxy; C₁-C₂₀ alkoxy; C₁-C₂₀ alkoxy;

C₁-C₂₀ alkylamino; C₁-C₂₀ alkylamino;

C₁-C₂₀ alkylcarboxylamino; aryl, aralkenoyl; carboxyl; cyano; halo;

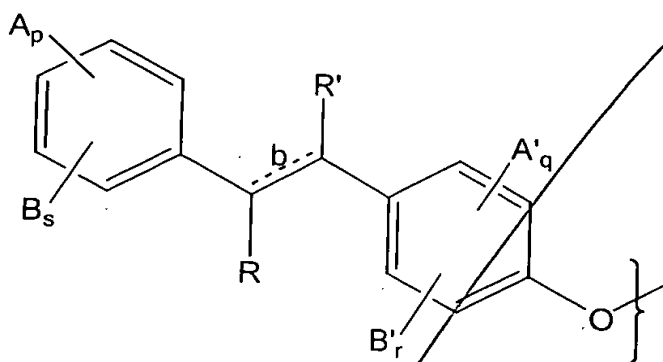
hydroxy;

or A and B together, or A' and B' together, or A'' and B'' together, may be joined to form a methylenedioxy or ethylenedioxy group; and

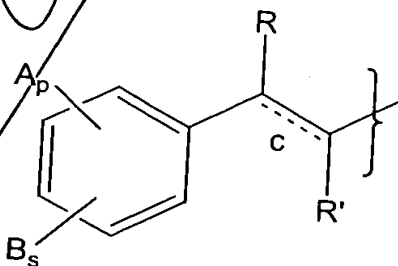
X, X' are independently -NH, -NR''', O or S,

in a physiologically acceptable carrier.

28. A method according to claim 27, wherein Z is



29. A method according to claim 27, wherein Z is H.
30. A method according to claim 27, wherein Z is A''.
31. A method according to claim 27, wherein Z is B''.
32. A method according to claim 27, wherein Z is



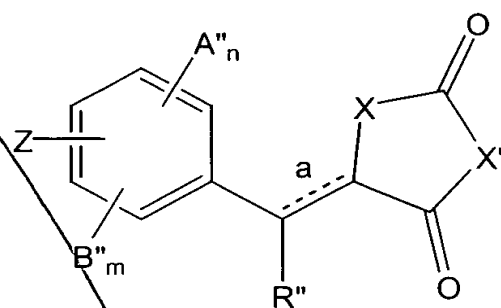
33. A method according to claim 27, wherein R'', A'', B'', A'_q, B', A_p and R are all hydrogen, X is sulfur and X' is NH.
34. A method according to claim 33, wherein R' is carbomethoxy and B is methoxy and s is 2.

35. A method according to claim 27⁴, wherein said compound is 5-(4-(4-(1-carbomethoxy-2-)3,5-dimethoxy phenyl) ethenyl)-phenoxy)-benzyl)-2,4-thiazolidinedione.

5 36. A method of treating immunological disease comprising the steps of administering to a subject suffering from an immunological disease, a therapeutically effective amount of a compound according to the formula I:

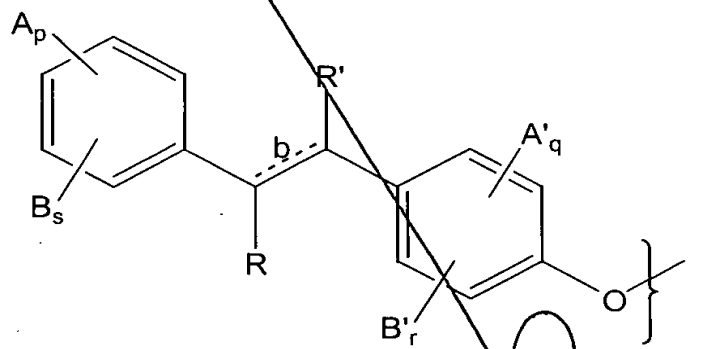
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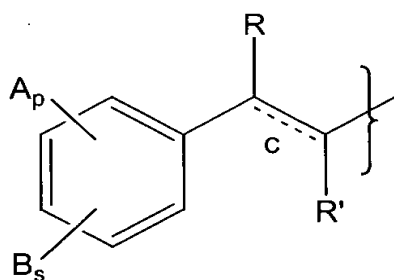


(I)

wherein Z is



H; A''; B''; or



- n, m, q and r are independently integers from zero to 4 provided that $n + m \leq 4$ and $q + r \leq 4$; p and s are independently integers from zero to 5 provided that $p + s \leq 5$; a, b and c are double bonds which may be present or absent;
 5 when present, the double bonds may be in the E or Z configuration and when absent, the resulting stereocenters may have the R- or S- configuration;

5 R, R' and R'' are independently H, C₁-C₂₀ linear or branched alkyl, C₂-C₂₀ linear or branched alkenyl, -CO₂Z', where Z' is H, sodium, potassium, or other pharmaceutically acceptable counter-ion such as calcium, magnesium, ammonium, tromethamine, and the like; -CO₂R''', -NH₂, -NHR''', -NR₂'', -OH, -OR''', halo, substituted C₁-C₂₀ linear or branched alkyl or substituted C₂-C₂₀ linear or branched alkenyl, wherein R''' is C₁-C₂₀ linear or branched alkyl or linear or branched alkenyl;

10 A, A' and A'' are independently H, C₁-C₂₀ acylamino;

C₁-C₂₀ acyloxy; C₁-C₂₀ alkanoyl;

C₁-C₂₀ alkoxycarbonyl; C₁-C₂₀ alkoxy;

C₁-C₂₀ alkylamino; C₁-C₂₀ alkylcarboxylamino; carboxyl; cyano;

halo; hydroxy;

15 B, B' and B'' are independently H,

C₁-C₂₀ acylamino; C₁-C₂₀ acyloxy; C₁-C₂₀ alkanoyl;

C₁-C₂₀ alkenoyl; C₁-C₂₀ alkoxycarbonyl;

C₁-C₂₀ alkoxy; C₁-C₂₀ alkylamino;

C₁-C₂₀ alkylcarboxylamino; aroyl, aralkanoyl; carboxyl; cyano; halo;

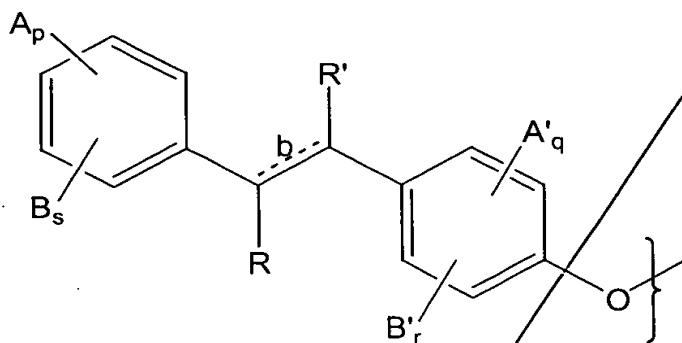
20 hydroxy;

or A and B together, or A' and B' together, or A'' and B'' together, may be joined to form a methylenedioxy or ethylenedioxy group; and

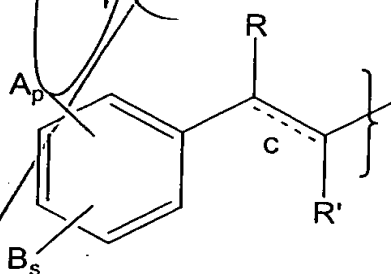
X, X' are independently -NH, -NR''', O or S,

in a physiologically acceptable carrier.

25 37. A method according to claim 36, wherein Z is



38. A method according to claim 36, wherein Z is H.
39. A method according to claim 36, wherein Z is A''.
40. A method according to claim 36, wherein Z is B''.
41. A method according to claim 36, wherein Z is



42. A method according to claim 36, wherein R'', A'', B'', A'_q, B', A_p and R are all hydrogen, X is sulfur and X' is NH.

43. A method according to claim 42, wherein R' is carbomethoxy and B is methoxy and s is 2.

44. A method according to claim 36, wherein said compound is 5-(4-(4-(1-carbomethoxy-2-)3,5-dimethoxy phenyl) ethenyl)-phenoxy)-benzyl)-2,4-thiazolidinedione.

5 45. A method of inhibiting the activity of TNF-alpha, IL-1, IL-6 or COX-2 which comprises administering to a host in need of such inhibition an effective amount of a compound according to claim 1.

10 46. The method of treating inflammation, inflammatory or immunological disease which comprises administering to a host in need of such treatment an effective amount of a compound according to claim 1.

15 47. The method of inhibiting the undesired action of cytokine or cyclooxygenase which comprises administering to a host in need of such inhibition an effective amount of a compound according to claim 1.

20 48. The method of treating an inflammatory disease mediated by cytokines or cyclooxygenase which comprises administering to a host in need of such treatment a compound according to claim 1.

25 49. The method of treating insulin resistance which comprises administering to a host in need of such treatment an effective amount of a compound according to claim 1.

50. The method of treating hyperlipidemia which comprises administering to a host in need of such treatment an effective amount of a compound according to claim 1.

30 51. The method of treating coronary heart disease which comprises administering to a host in need of such treatment an effective amount of a compound according to claim 1.

52. The method of treating multiple sclerosis which comprises administering to a host in need of such treatment an effective amount of a compound according to claim 1.

53. The method of treating cancer which comprises administering to a host in need of such treatment an effective amount of a compound according to claim 1.

54. The method of claim 45, 46, 47, 48, 49, 50, 51, 52 or 53 wherein the compound is 5-(4-(4-(1-carbomethoxy)-2-(3,5-dimethoxyphenyl)-ethenyl)-phenoxy)-benzyl)-2,4-thiazolidinedione.

55. A compound according to claim 1 selected from the group consisting of:

3-(3,5-dimethoxyphenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-acrylic acid,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-acrylamide,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-N,N-dimethyl-acrylamide,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-N-methoxy,-N-methyl-acrylamide,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-phenoxy]-phenyl}-propionic acid methyl ester,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-phenoxy]-phenyl}-acrylic acid methyl ester,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-propionic acid,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-phenoxy]-phenyl}-propionic acid,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-
phenoxy]-phenyl}-acrylic acid, and
3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-
phenyl}-propionic acid methyl ester.

5

56. A compound according to claim 1 which is 3-(3,5-dimethoxyphenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-acrylic acid.

10

57. A pharmaceutical composition comprising a therapeutically effective amount of a compound selected from the group consisting of 3-(3,5-dimethoxyphenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-acrylic acid,

15

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-acrylamide,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-N,N-dimethyl-acrylamide,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-N-methoxy,-N-methyl-acrylamide,

20

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-phenoxy]-phenyl}-propionic acid methyl ester,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-phenoxy]-phenyl}-acrylic acid methyl ester,

25

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-propionic acid,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-phenoxy]-phenyl}-propionic acid,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-phenoxy]-phenyl}-acrylic acid, and

30

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-propionic acid methyl ester,

together with a physiologically acceptable carrier therefor.

58. The pharmaceutical composition of claim 57 wherein said compound is 3-(3,5-dimethoxyphenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-acrylic acid.

59. The method of claim 18, 45, 46, 47, 48, 49, 50, 51, 52 or 53 wherein said compound is selected from the group consisting of

3-(3,5-dimethoxyphenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-acrylic acid,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-acrylamide,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-N,N-dimethyl-acrylamide,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-N-methoxy,-N-methyl-acrylamide,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-phenoxy]-phenyl}-propionic acid methyl ester,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-phenoxy]-phenyl}-acrylic acid methyl ester,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-propionic acid,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-phenoxy]-phenyl}-propionic acid,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-phenoxy]-phenyl}-acrylic acid, and

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-propionic acid methyl ester.

60. The method of claim 59 wherein the compound is 3-(3,5-dimethoxyphenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-acrylic acid.

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B

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Ca

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